

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.

1. Use of at least one fragment of an enterobacterium membrane protein OmpA for preparing a pharmaceutical composition intended to be administered nasally, to improve the immunity of a mammal with respect to an antigen or to a hapten.

5 2. Use of at least one fragment of a membrane protein of Klebsiella for preparing a pharmaceutical composition intended to be administered nasally, to improve the immunity of a mammal with respect to an antigen or to a hapten.

10 3. Use of at least one fragment of a membrane protein according to claim 2, characterized in that the membrane protein is an OmpA of Klebsiella pneumoniae.

15 4. Use of at least one fragment of a membrane protein according to one of claims 1 to 3, characterized in that said membrane protein or its fragment is obtained by recombinant process.

20 5. Use of at least one fragment of a membrane protein according to claim 4, characterized in that said recombinant membrane protein or its fragment is renatured in the presence of detergent chosen from Zwittergent 3-14, Zwittergent 3-12 and octylglucopyranoside.

25 6. Use of at least one fragment of a membrane protein according to one of claims 1 to 5, characterized in that at least one fragment has the sequence SEQ ID No 1.

30 7. Use according to one of claims 1 to 6, characterized in that the antigen or the hapten are chosen from the group comprising proteins, peptides, polysaccharides, oligosaccharides and nucleic acids.

35 8. Use of at least one fragment of a membrane protein according to one of claims 1 to 7, characterized in that the antigen or the hapten originate from a virus or from a bacterium.

9. Use of at least one fragment of a membrane protein according to one of claims 1 to 8,

characterized in that the antigen or the hapten comprises at least one protein fragment of a microorganism responsible for pathologies of the airways.

5 10. Use according to claim 9, characterized in that said microorganism responsible for pathologies of the airways is chosen from RSV, parainfluenzae virus (PIV), influenza virus, hantavirus, streptococci, pneumococci and meningococci.

10 11. Use of at least one fragment of a membrane protein according to one of claims 1 to 10, characterized in that the antigen or the hapten comprises at least one protein fragment of the human or bovine respiratory syncytial virus (RSV).

15 12. Use according to claim 11, characterized in that the antigen or hapten comprises at least one fragment of the protein G of the RSV.

13. Use according to either of claims 11 and 12, characterized in that the antigen or the hapten

20 20. comprises at least one of the sequences SEQ ID No 2 to SEQ ID No 74.

25 14. Use according to one of claims 1 to 13, characterized in that said fragment of a membrane protein is covalently coupled to said antigen or hapten.

15. Use according to claim 14, characterized in that one or more bonding elements is introduced into the fragment of membrane protein and/or of the antigen or of the hapten in order to facilitate the coupling.

30 16. Use according to claim 15, characterized in that the bonding element introduced is an amino acid.

17. Use according to claim 14, characterized in that the hybrid protein, which is obtained after coupling between the fragment of a membrane protein and the antigen or the hapten, when said antigen or hapten is protein in nature, is prepared by genetic recombination.

35 18. Use according to one of claims 14 to 17, characterized in that the pharmaceutical composition

- 18 -
76 18

contains a fragment of a membrane protein coupled to an antigen or a hapten.

19. Use according to claim 17, characterized in that the pharmaceutical composition contains a transformed host cell which is capable of expressing a hybrid protein containing said fragment of membrane protein coupled to said antigen or hapten.

5 20. Use according to either of claims 18 and 19, characterized in that the pharmaceutical composition 10 does not contain any adjuvant.

15 21. Method for preparing a protein or one of its fragments by recombinant process, characterized in that said protein or one of its fragments is, after extraction, renatured in the presence of a solution comprising a detergent chosen from Zwittergent 3-14, Zwittergent 3-12 and octylglucopyranoside, and in that said recombinant protein is not interferon β .

- 22 -

Use of at least one fragment of a membrane protein for preparing a pharmaceutical composition intended to be administered nasally, selected from the group consisting of an enterobacterium membrane protein, an enterobacterium membrane protein OmpA, a Klebsiella membrane protein, and a Klebsiella pneumonia membrane protein OmpA useful for improving immunity of a mammal with respect to an antigen or a hapten.

- 23 -

Use of Claim 22 wherein the membrane protein or its fragment is obtained by recombinant process.

- 24 -

Use of Claim 23 wherein the recombinant membrane protein or its fragment is renatured in the presence of a detergent selected from Zwittergent 3-14, Zwittergent 3-12, and octylglucopyranoside.

- 25 -

Sub B
Use of Claim 22 wherein at least one fragment has the sequence SEQ ID No 1.

- 26 -

Use of Claim 22 wherein the antigen or hapten are selected from the group consisting of proteins, peptides, polysaccharides, oligosaccharides and nucleic acids.

- 27 -

Use of Claim 26 wherein the antigen or hapten originate from a virus or a bacterium.

- 28 -

Use of Claim 27 wherein the antigen or hapten comprise at least one protein fragment of a microorganism responsible for pathologies of the airways.

- 29 -

Use of Claim 28 wherein the microorganism is selected from the group consisting of RSV, parainfluenza virus (PIV), influenza virus, hantavirus, streptococci, pneumococci and meningococci.

- 30 -

Use of Claim 26 wherein the antigen or hapten comprises at least one protein fragment of the human or bovine respiratory syncytial virus (RSV).

- 31 -

Use of Claim 30 wherein the antigen or hapten comprises at least one fragment of the G protein of the RSV.

- 32 -

Sub B2
Use of Claim 30 wherein the antigen or hapten comprises at least one of sequences SEQ ID No 2 through SEQ ID No 74.

- 33 -

Use of Claim 31 wherein the antigen or hapten comprises at least one of sequences SEQ ID No 3 through SEQ ID No 136.

- 34 -

Use of Claim 22 wherein the membrane protein or its fragment is covalently coupled to the antigen or hapten.

- 35 -

Use of Claim 34 wherein one or more bonding elements is introduced into the membrane protein or its fragment and/or introduced into the antigen or hapten to facilitate the coupling, forming a hybrid protein.

- 36 -

Use of Claim 35 wherein the bonding element introduced is an amino acid.

- 37 -

Use of Claim 36 wherein the hybrid protein, obtained after coupling between the membrane protein or its fragment and the antigen or hapten, wherein the antigen or hapten is protein in nature, is prepared by genetic recombination.

- 38 -

Use of Claim 37 including a transformed host cell which is capable of expressing a hybrid protein containing said fragment of membrane protein coupled to said antigen or hapten.

- 39 -

Use of Claim 38 which does not contain an adjuvant.

- 40 -

A method of preparing a protein or one of its fragments by recombinant process, wherein said protein or one of its fragments is, after extraction, renature in the presence of a solution comprising a detergent chosen from Zwittergent 3-14, Zwittergent 3-12 and octylglucopyranoside, and wherein said recombinant protein is not interferon β .